

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A bovine ~~comprising whose genome comprises~~ a non-naturally occurring mutation in one or both alleles of an endogenous prion nucleic acid, wherein said bovine exhibits reduced functional prion production.

2-3. (Cancelled).

4. (Original) The bovine of claim 1, wherein said mutation is hemizygous.

5. (Currently amended) The bovine of claim 1, wherein said mutation is homozygous and said bovine exhibits no functional prion production.

6. (Original) The bovine of claim 1, wherein said mutation comprises an insertion of a positive selection marker into a prion nucleic acid.

7. (Withdrawn) The bovine of claim 1, wherein said mutation comprises an insertion of a STOP codon into a prion nucleic acid.

8. (Withdrawn) The bovine of claim 1, wherein said mutation comprises a deletion of one or more nucleotides in a prion nucleic acid.

9. (Withdrawn) The bovine of claim 1, comprising one or more nucleic acids comprising one or more transgenes and expressing an mRNA or protein encoded by said transgene(s).

10. (Withdrawn) The bovine of claim 1, comprising one or more nucleic acids comprising all or part of a xenogenous immunoglobulin (Ig) gene which undergoes rearrangement and expresses more than one xenogenous Ig molecule.

11. (Withdrawn) The bovine of claim 10, comprising one or more nucleic acids encoding a xenogenous antibody.

12. (Withdrawn) The bovine of claim 11, wherein said xenogenous antibody is a human antibody.

13. (Withdrawn) The bovine of claim 12, wherein said antibody is expressed in serum and/or milk.

14. (Withdrawn) The bovine of claim 1, comprising a mutation that reduces the expression of an endogenous antibody.

15. (Withdrawn) The bovine of claim 14, wherein said mutation reduces the expression of functional IgM heavy chain.

16. (Withdrawn) The bovine of claim 15, wherein said mutation substantially eliminates the expression of functional IgM heavy chain.

17. (Withdrawn) The bovine of claim 14, wherein said mutation reduces the expression of functional Ig light chain.

18. (Withdrawn) The bovine of claim 17, wherein said mutation substantially eliminates the expression of functional Ig light chain.

19. (Withdrawn) The bovine of claim 14, wherein said mutation reduces the expression of functional IgM heavy chain and functional Ig light chain.

20. (Withdrawn) The bovine of claim 19, wherein said mutation substantially eliminates the expression of functional IgM heavy chain and functional Ig light chain.

21. (Withdrawn) The bovine of claim 1, comprising a mutation in one or both alleles of an endogenous nucleic acid encoding alpha-(1,3)-galactosyltransferase.

22. (Withdrawn) The bovine of claim 1, comprising a mutation in one or both alleles of an endogenous nucleic acid encoding J chain.

23. (Withdrawn) The bovine of claim 1, comprising a nucleic acid encoding an exogenous J chain.

24. (Withdrawn) The bovine of claim 23, wherein said J chain is a human J chain.

25. (Currently amended) A bovine cell comprising a non-naturally occurring mutation in one or both alleles of an endogenous prion nucleic acid, wherein said bovine cell exhibits reduced functional prion production.

26-27. (Cancelled).

28. (Original) The cell of claim 25, wherein said mutation is hemizygous.

29. (Currently amended) The cell of claim 25, wherein said mutation is homozygous and said bovine cell exhibits no functional prion production.

30. (Original) The cell of claim 25, wherein said cell is a fetal fibroblast.

31. (Original) The cell of claim 25, wherein said cell is a B-cell.

32. (Currently amended) A method for producing [[a]] an isolated transgenic bovine cell having reduced expression of functional prion protein, comprising

(a) introducing a first prion gene targeting vector into a bovine cell under conditions that allow homologous recombination between said first vector and a first allele of an endogenous prion nucleic acid in said cell, thereby introducing a hemizygous mutation in said cell;

(b) isolating said bovine cell containing hemizygous mutation; and

(c) introducing a second prion gene targeting vector having a different selectable marker than said first vector into said bovine cell of step (b) under conditions that allow homologous recombination between said second vector and a second allele of an endogenous prion nucleic acid in said cell, thereby introducing a homozygous mutation in said bovine cell.

33-34. (Cancelled).

35. (Original) The method of claim 32, wherein said cell is a bovine fibroblast.

36. (Original) The method of claim 35, wherein said cell is a bovine fetal fibroblast.

37. (Currently amended) A method for producing a transgenic bovine having reduced expression of functional prion protein, said method comprising the steps of:

(a) inserting a diploid permeabilized cell, a chromatin mass from a cell, or a nucleus from a cell into an enucleated metaphase II oocyte, wherein said cell comprises a first non-naturally occurring mutation in an endogenous prion nucleic acid; and

(b) transferring said oocyte or an embryo formed from said oocyte into the uterus of a host bovine under conditions that allow said oocyte or said embryo to develop into a

fetus, wherein the genome of said fetus comprises said non-naturally occurring mutation in said endogenous prion nucleic acid and wherein said fetus exhibits reduced functional prion production.

38. (Original) The method of claim 37, wherein said fetus develops into a viable offspring.

39. (Cancelled).